HOW TO GIVE PRILACTONE® ALONGSIDE OTHER HEART FAILURE MEDICATIONS

- Prilactone® should be added to your preferred first-line treatment regime for canine heart failure.
- Tolerance studies have shown that Prilactone® can be safely combined with existing heart failure therapies, including:
  - Pimobendan
  - ACE Inhibitors
  - Furosemide
- Furosemide is essential for the treatment of pulmonary oedema but may actually stimulate aldosterone production, as shown by the following studies:
  - In healthy dogs, 10 days of furosemide (at 2mg/kg BID), with or without pimobendan (at 0.25mg/kg BID) was shown to cause a three-fold increase in urinary aldosterone secretion.
  - In healthy dogs and dogs with congestive heart failure caused by mitral valve disease, furosemide was shown to stimulate aldosterone production even though these dogs were receiving an ACE inhibitor (aldosterone escape).

REFERENCES

6. Falk P. et al. (2007), Cardiac fibrosis, correlation of cardiac fibrosis and clinical findings in dogs with naturally occurring congestive heart failure, ACRM abstracts, 253-260.
Heart failure causes a reduction in cardiac output and a decrease in renal perfusion. This results in the release of renin from the kidney which, in turn, converts angiotensinogen into angiotensin I.

Angiotensin Converting Enzyme (ACE) then converts angiotensin I into angiotensin II.

Angiotensin II, in turn, stimulates the release of aldosterone from the adrenal gland. However, in dogs and man, aldosterone has been shown to increase despite ACE inhibition. This is thought to be because other factors, such as K⁺ and ACTH, can also stimulate aldosterone production.

Aldosterone is also produced locally by the heart and blood vessels and this is thought to be independent to control by circulating angiotensin II.

Aldosterone binds to mineralocorticoid receptors, which are located within the myocardium, and causes myocardial fibrosis.

Prilactone® blocks the mineralocorticoid receptors on the heart, and therefore protects against the development of myocardial fibrosis.
Reduce fibrosis
Prolong life

Anti-fibrotic effect demonstrated in the dog

Complete your first-line therapeutic approach to canine mitral valve disease
CARDIAC FIBROSIS DURING HEART FAILURE

HEALTHY HEART MUSCLE

• The healthy heart muscle (myocardium) contains an extracellular collagen matrix (ECCM), which provides structural support

• Normal cardiac function relies on contraction and relaxation of the myocardium

HEART FAILURE AND MYOCARDIAL FIBROSIS

• In dogs suffering from congestive heart failure, excessive collagen becomes deposited within the myocardium and the amount of healthy heart muscle is reduced. This is known as myocardial fibrosis (figure 1)

• Myocardial fibrosis contributes to the progression of heart disease
  - Stiffens the heart muscle
  - abnormal myocardial contraction and relaxation
  - Increases mitral regurgitation
  - Predisposes to the development of arrhythmias

THE LINK BETWEEN MYOCARDIAL FIBROSIS AND MORTALITY RISK

• In human patients with heart failure, myocardial fibrosis is associated with significantly increased mortality

• Similarly, dogs with mitral valve disease have significantly more myocardial fibrosis and the greater the degree of fibrosis, the shorter the survival time (figure 2)
**THE LINK BETWEEN ALDOSTERONE AND MYOCARDIAL FIBROSIS**

**ALDOSTERONE AND HEART FAILURE**

- Aldosterone works by binding to Mineralocorticoid Receptors, which are present throughout the body, including within the myocardium (see figure 3).
- In healthy mammals, aldosterone is produced in small quantities and helps to regulate electrolyte and fluid balance.
- In dogs suffering from congestive heart failure, a three-fold increase in plasma aldosterone concentration occurs giving rise to pathological hyperaldosteronism.
- Chronically high aldosterone levels cause myocardial fibrosis.
- In dogs with mitral valve disease, aldosterone has been linked to an increase in ventricular remodelling and reduced survival.

**ALDOSTERONE ANTAGONISTS REDUCE FIBROSIS AND IMPROVE SURVIVAL**

- Prilactone® is an aldosterone antagonist which works by blocking Mineralocorticoid Receptors (figure 4).
- Aldosterone antagonists have been shown to reduce myocardial fibrosis.
- In human patients, aldosterone antagonists have a class 1 indication in both European and US guidelines for the treatment of heart failure as a result of significant reductions in the risk of mortality and hospitalisation rates (figure 5).
- Similarly in dogs with mitral valve disease, a new publication has demonstrated a significant 69% reduction in the risk of mortality when Prilactone® was added as part of first-line therapy for congestive heart failure.

![Figure 3: Aldosterone binds to mineralocorticoid receptors present within the myocardium](image)

![Figure 4: Prilactone® blocks the mineralocorticoid receptors within the myocardium](image)

![Figure 5: Kaplan-Meier survival curves for human patients in the placebo group and those in the spironolactone group](image)
NEW PUBLICATION HIGHLIGHTS THE BENEFITS OF PRILACTONE® IN DOGS

Bernay F. et al. (2010), Efficacy of Spironolactone on Survival in Dogs with Naturally-occurring Mitral Regurgitation caused by Myxomatous Mitral Valve Disease, Journal of Veterinary Internal Medicine, 24(2), 331 - 341.

STUDY DESIGN

- 15 month study
- Double-blind, placebo-controlled
- 212 dogs with first-line congestive heart failure caused by mitral valve disease
- Randomised groups received either:
  - ACE inhibitor, furosemide® and placebo OR
  - ACE inhibitor, furosemide® and Prilactone®

RESULTS

- 69% reduction in the risk of mortality from heart failure in Prilactone® group (p=0.0071, figure 6)

  *Increased probability of survival due to Prilactone®

- Statistically significant benefits in quality of life parameters in Prilactone® group (figure 7)

  *Increased probability of survival due to Prilactone®

- Extremely well tolerated - no increased risk of hyperkalaemia and excellent renal tolerance

This study clearly demonstrates that the addition of Prilactone® significantly reduces the risk of mortality and improves quality of life in dogs with mitral valve disease when added as part of first-line therapy for congestive heart failure.

*Furosemide usage/dose determined by the clinician according to the dog’s clinical needs. Other authorised treatments in both groups included digoxin and L-carnitine.